

REMARKS

Claims 1-9 and 25-29 are pending. Claims 10-24 were previously canceled. Claims 7-9 and 27 have been withdrawn by the Examiner as drawn to nonelected species. Applicant respectfully reminds the Examiner that upon finding allowable subject matter, applicant is entitled to have the withdrawn claims rejoined and considered in this application as provided by 37 C.F.R. 1.141. *See* M.P.E.P. § 809.02(a). Claims 1-6, 25, 26, 28, and 29 are under consideration.

In the present amendment, claim 1 has been amended to recite “a glycoprotein preparation having improved complement-dependent cytotoxicity activity” and “wherein the glycoprotein preparation has improved complement-dependent cytotoxicity activity compared to a preparation of that glycoprotein having heterogeneous oligosaccharide.” Support for those amendments is found in the specification, e.g., at page 8, lines 25-32. Additional amendments to claim 1 merely correct minor grammatical errors. Accordingly, no new matter has been added.

Rejection of Claims 1-6, 25, 26, 28, and 29 Under 35 U.S.C. § 103(a)

The Examiner has maintained the rejection of claims 1-6, 25, 26, 28, and 29 under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 4,859,449 issued to Mattes (“Mattes”), in view of Kumpel and Maras. Action at page 2, item no. 3.

In the Examiner’s view, Mattes teaches therapeutic antibodies with terminal galactose oligosaccharides and the uses/advantages of such antibodies. The Examiner acknowledges that Mattes does not teach that the antibodies are of the degree of purity recited in the claims. Nevertheless, the Examiner alleges that

[i]t would have been prima facie obvious to one of ordinary skill in the art to have created the claimed invention because Mattes teaches therapeutic antibodies with terminal galactose oligosaccharides and the uses/advantages of such antibodies whilst Kumpel teach that antibodies with substantially all G2 oligosaccharide

have increased lysis of target cells in comparison to the same antibody which is produced in a manner that results in low levels of G2 and Maras et al teach that B-1,4 Galactosyltransferase can be used to modify the oligosaccharide profile on a glycoprotein. . . .

Action at p. 3-4.

Applicant respectfully traverses the rejection. Claim 1 has been amended to recite “[a] therapeutic composition comprising a glycoprotein preparation having improved complement-dependent cytotoxicity activity, said glycoprotein having an immunoglobulin CH2 domain and said CH2 domain having at least one N-linked oligosaccharide, wherein substantially all of the oligosaccharide is a G2 oligosaccharide and wherein the amount of said glycoprotein containing G1 and G0 oligosaccharide does not exceed 10% by weight of the preparation, and wherein the glycoprotein preparation has improved complement-dependent cytotoxicity activity compared to a preparation of that glycoprotein having heterogeneous oligosaccharide.” As explained further below, there is simply no teaching or suggestion in Mattes, nor in any combination of Mattes with Kumpel and/or Maras of the claimed glycoproteins having improved complement-dependent cytotoxicity activity.

Mattes is directed to methods of modifying antibodies for therapeutic and diagnostic purposes such that they are cleared more rapidly from the circulation. *See, e.g.*, Mattes at abstract and col. 2, lines 3-17. According to Mattes, such antibodies are “conjugated to, or [have] exposed thereon, a plurality of terminal glycoside residues which bind to the human hepatocyte asialoglycoprotein receptor.” Mattes at col. 2, lines 37-39.

While Mattes does discuss that one may “expos[e] such glycosides as terminal residues on existing, complex carbohydrates on the antibody,” and notes that such “glycosides can be exposed on the surface of an antibody by suitable treatment,” e.g., by using neuraminidases (*See, e.g.*, col. 6, lines 21-26 and at lines 47-57), and while Mattes refers in the background section to

the complement-mediated cytotoxicity effect of antibodies in general (*see, e.g.*, col. 1, lines 28-31), Mattes is completely silent regarding the effects on complement-dependent cytotoxicity (CDC) activity of the antibody conjugates discussed therein. None of the examples investigate CDC activity nor does Mattes discuss or suggest anywhere that CDC activity may be improved by any of the disclosed antibody conjugates.

Kumpel fails to cure the deficiencies of Mattes. While Kumpel does discuss the effects of the antibodies described therein on antibody-dependent cell-mediated cytotoxicity (ADCC) (*see, e.g.*, abstract), Kumpel is completely silent regarding the effects, if any, on CDC activity. And nowhere does Kumpel discuss or suggest that any of the antibodies described therein may have improved CDC activity. Applicant notes that it is well known in the art that the ADCC mechanism and the CDC mechanism resulting in cell lysis are different mechanisms involving, *e.g.*, different receptors. *See, e.g.*, Mattes at col. 1, lines 28-31 and the present specification at p. 3, lines 9-12. Accordingly, Kumpel's statements concerning the effects of the antibodies described therein on ADCC activity refer only to ADCC activity and do not in any way implicate CDC activity.

Maras also fails to cure the deficiencies Mattes as well as Kumpel. Maras is completely silent about CDC activity of any of the glycoproteins described therein.

Accordingly, there is simply no teaching or suggestion in any one or combination of Mattes, Kumpel or Maras of "[a] therapeutic composition comprising a glycoprotein preparation having improved complement-dependent cytotoxicity activity, said glycoprotein having an immunoglobulin CH2 domain and said CH2 domain having at least one N-linked oligosaccharide, wherein substantially all of the oligosaccharide is a G2 oligosaccharide and wherein the amount of said glycoprotein containing G1 and G0 oligosaccharide does not exceed

10% by weight of the preparation, and wherein the glycoprotein preparation has improved complement-dependent cytotoxicity activity compared to a preparation of that glycoprotein having heterogeneous oligosaccharide,” according to claim 1. Accordingly, claim 1 would not have been obvious in view of Mattes, Kumpel and/or Maras. Each of claims 2-6, 25, 26, 28, and 29 ultimately depend from claim 1 or otherwise include all the elements of claim 1. Therefore, none of the dependent claims would have been obvious in view of Mattes, Kumpel and/or Maras. Therefore, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 1-6, 25, 26, 28, and 29 under 35 U.S.C. § 103(a) as allegedly being obvious in view of Mattes, Kumpel and/or Maras.

Because claims 1-6, 25, 26, 28, and 29 would not have been obvious for at least the reasons discussed above, Applicant need not address the Examiner’s contentions concerning other elements of those claims. By not addressing those contentions, applicant in no way acquiesces to those contentions.

CONCLUSION

Applicant respectfully asserts that the claims are in condition for allowance and requests the timely issuance of a Notice of Allowance. Should the Examiner believe that a telephone interview would expedite the prosecution of this application, applicant invites the Examiner to call the undersigned at the telephone number indicated below.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 07-0630.

Respectfully submitted,
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